

We claim:

1. A de-immunized anti-CD3 antibody.

2. A de-immunized anti-CD3 antibody heavy chain variable region

comprising a sequence selected from the group consisting of SEQ. ID NOS: 11, 12, 13, 14, 15, 16 and 17.

3. A de-immunized anti-CD3 antibody light chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 19 and 20.

4. A method comprising:

selecting an anti-CD3 antibody; and

rendering the anti-CD3 antibody less immunogenic to a given species.

5. A method as in claim 4 wherein the step of rendering the anti-CD3 antibody less immunogenic to a given species comprises the steps of:

(a) determining at least part of the amino acid sequence of the antibody;

(b) identifying in the amino acid sequence one or more potential epitopes for T cells ("T cell epitopes") which are found in an endogenous protein of the given species; and

(c) modifying the amino acid sequence to eliminate at least one of the T cell epitopes identified in step (b) thereby to reduce the immunogenicity of the antibody or part thereof when exposed to the immune system of the given species.

6. A method comprising the steps of:

- (a) producing an expression vector having a DNA sequence which includes a sequence that encodes an anti-CD3 antibody, at least a portion of which has been de-immunized;
- (b) transfecting a host cell with the vector; and
- (c) culturing the transfected cell line to produce a de-immunized anti-CD3 antibody molecule.

7. A pharmaceutical composition comprising a de-immunized anti-CD3 antibody and a pharmaceutically acceptable carrier.

8. A composition as in claim 7 wherein the de-immunized anti-CD3 antibody includes a heavy chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 11, 12, 13, 14, 15, 16 and 17.

9. A composition as in claim 7 wherein the de-immunized anti-CD3 antibody includes a light chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 19 and 20.

10. A method comprising administering an anti-CD3 antibody, the anti-CD3 antibody including an engineered heavy chain constant region having a first portion derived from one or more human IgG2 antibodies and a second portion derived from

one or more human IgG4 antibodies, at least a portion of the antibody being de-immunized.

11. A method as in claim 10 wherein at least the light chain variable region of the antibody is de-immunized.

12. A method as in claim 10 wherein at least the heavy chain variable region of the antibody is de-immunized.

13. A method as in claim 10 wherein both the light and heavy chain variable regions of the antibody are de-immunized.

14. A method as in claim 10 wherein the anti-CD3 antibody includes a heavy chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 11, 12, 13, 14, 15, 16 and 17.

15. A method as in claim 10 wherein the anti-CD3 antibody includes a light chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 19 and 20.

16. A method as in claim 10 wherein at least a portion of the antibody is de-immunized by a process comprising the steps of:
rendering the antibody, or part thereof, non-immunogenic, or less immunogenic,

to a given species by

- a) determining at least part of the amino acid sequence of the antibody;
- (b) identifying in the amino acid sequence one or more potential epitopes for T cells ("T cell epitopes") which are found in an endogenous protein of the given species; and
- (c) modifying the amino acid sequence to eliminate at least one of the T cell epitopes identified in step (b) thereby to reduce the immunogenicity of the antibody or part thereof when exposed to the immune system of the given species.

17. Nucleic acid encoding a de-immunized anti-CD3 antibody.

18. Nucleic acid in accordance with claim 17 which encodes an antibody heavy chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 11, 12, 13, 14, 15, 16 and 17.

19. Nucleic acid in accordance with claim 17 which encodes an antibody light chain variable region comprising a sequence selected from the group consisting of SEQ. ID NOS: 19 and 20.

20. A pharmaceutical composition comprising an anti-CD3 antibody encoded by the nucleic acid in accordance with any of claims 17 through 19 and a pharmaceutically acceptable carrier.